

AMENDMENTS TO THE SPECIFICATION:

Please delete the paragraph on page 1, lines 2-6, and substitute therefor the following new paragraph:

-- The present invention relates to a diagnostic method for paratuberculosis (Johne's disease), and more specifically to improvement of the sensitivity, to application in an early stage of the infection before increase of the specific antibody and to use large scale field application. --

Please delete the paragraph on page 1, lines 8-15, and substitute therefor the following new paragraph:

-- Paratuberculosis is caused by *Mycobacterium avium* subsp. *paratuberculosis* that is one of acid-fast bacteria, and is a chronic granulomatous diarrheal infectious disease in ruminants such as cattle, goats, sheep, and buffalos. With regard to pandemic of bovine paratuberculosis in Japan, theby increase of infected animals and the expansion of~~expand~~ the outbreak areas have been seen since 1980. In particular, the outbreak numbers increased at a rate of 100 to 200 cattle/year from the 1990s, and exceeded 800 in 2000. --

Please delete the paragraph beginning on page 1, line 16 through page 2, line 2, and substitute therefor the following new paragraph:

-- Fig. 1 shows the course of infection (from infection to onset of symptoms) of ~~paratuberculosis~~paratuberculosis and shift in immune response. ~~Paratuberculosis~~Paratuberculosis is developed by oral infection of *Mycobacterium avium* subsp. *paratuberculosis* in the early period after birth. However, most of the

routes of infection ~~are~~is still unclear, and differences in the course of the disease between individuals are larger than those in any other diseases. --

Please delete the paragraph on page 2, lines 9-22, and substitute therefor the following new paragraph:

-- The ELISA method is a diagnostic method involving detecting a specific antibody against *Mycobacterium avium* subsp. *paratuberculosis*, and is prevalent~~prevailed~~ all over the world because of its simplicity (see Momotani Eiichi "Up-to-date information on diagnosis of bovine Johne's disease", Journal of Clinical Veterinary Medicine, vol. 16 (9), 1998, 24-31, in Japanese). However, the method can be used in diagnosing cattle in advanced stage, or after increase of antibody level, but cannot diagnose sub-clinically infected animals before the specific antibody level increases. However, as a result of prevalence of this ELISA method as a standard for diagnosis of paratuberculosis, sub-clinically infected animals that cannot be diagnosed by the ELISA method relatively increases, although ELISA-positive cattle decreases. Therefore, the diagnosis becomes increasingly harder. --

Please delete the paragraph beginning on page 2, line 23 through page 3, line 4, and substitute therefor the following new paragraph:

-- Meanwhile, as shown in Fig. 1, the cell-mediated immunity of an animal infected with *Mycobacterium avium* subsp. *paratuberculosis* is induced at the early stage of infection but is then gradually decreased. Examples of diagnostic methods of such cell-mediated immunity include a johnin reaction and an interferon γ (IFN γ) ELISA method. --

Please delete the paragraph on page 6, lines 10-17, and substitute therefor the following new paragraph:

-- However, the method requires several months to culture *Mycobacterium avium* subsp. *paratuberculosis* in order until to recognize the bacterial colonies. Therefore, it is difficult to diagnose the infection at an early stage, and there is a problem in that the infection is spread owing to excretion of the bacteria from a carrier animal animals during culture. Meanwhile, excretion of the bacteria occurs irregularly and nonpersistently, so there is also a problem in that some infected individuals are not accurately diagnosed. --

Please delete the paragraph on page 13, lines 10-22, and substitute therefor the following new paragraph:

-- The term "subject animal" means an animal that may be infected with *Mycobacterium avium* subsp. *paratuberculosis* and is subjected to a diagnostic method of the present invention. Examples of the animal include ruminants such as cattle (in which contamination of paratuberculosis is spreading in Japan), sheep, goats, and buffalos. Moreover, examples thereof include animals other than the ruminants such as wild deer and animals related to cattle (artiodactyls), which have been reported to be infected with paratuberculosis. Furthermore, in the case where the method is intended for human as a targeted subject animal, it can also be revealed that ~~involvement of~~ a *Mycobacterium avium* subsp. *paratuberculosis* antigen is involved in human Crohn's disease (intractable disease designated by Ministry of Health, Labour and Welfare). --

Please delete the paragraph beginning on page 15, line 22 through page 16, line 3, and substitute therefor the following new paragraph:

-- *Mycobacterium avium* subsp. *paratuberculosis* PPD may be prepared in accordance with a method described in, for example, Manual of Standards for Diagnostic Protocols (Office International des Epizooties (OIE) .2000. Manual of standards for diagnostic tests and vaccines. *Paratuberculosis* (Johne' s disease). <http://www.oie.int/esp/normes/mmanual/ancienmanuel/a00043.htm>). --

Please delete the paragraph on page 24, lines 9-16, and substitute therefor the following new paragraph:

-- Before adding an anti-IL-10 antibody and *Mycobacterium avium* subsp. *paratuberculosis* PPD to the collected peripheral blood followed by culture, first, *Mycobacterium avium* subsp. *paratuberculosis* PPD was prepared in accordance with "Manual of Standards for Diagnostic Protocols (Office International des Epizooties (OIE) .2000. Manual of standards for diagnostic tests and vaccines. *Paratuberculosis* (Johne's disease). http://www.oie.int/eng/normes/mmanual/A_00043.htm). --